DETAILED ACTION

1. Applicant's claims amendments, remarks and election of species, without traverse, filed May 18, 2011 is acknowledged.

2. Applicant's papers filed May 18, 2011 were in response to the restriction requirement mailed April 18, 2011 which was induced by applicant's claim amendments filed October 27, 2010.

   As stated in the restriction requirement mailed April 18, 2011, "[t]he claims as amended appear to no longer encompass in their breadth the prior elected species of 'culture conditions for the ex vivo education of NKT'…"

   In particular as further described in the restriction requirement mailed April 18, 2011:

   "…the vast majority of the claims seem to limit the claimed methods to using 'proteins extracted from tissue…' **OR** 'at least one liver-associated cell…' to educate / modulate the NKT cells it will be assumed that this is what applicant intends to claim.

   Thus, by the claim amendments filed October 27, 2010 applicant has deleted the prior elected species of 'culture conditions for the ex vivo education of NKT' which used 'allogeneic antigens obtained from donors suffering from said immune-related or immune-mediated disease', 'Kupffer cells' and 'IL4' from the breadth of the claimed method. Rather, the claims as amended now encompass the species of method employing 'culture conditions for the ex vivo education of NKT' which use ***either*** 'proteins extracted from tissue affected by the immune- related disorder' ***OR*** 'at least one liver-associated cell of tolerized or non-tolerized subjects suffering from said immune-related or immune-mediated disorder or of said subject.'

   Given this fact pattern and the guidance presented in the final paragraph of MPEP § 821.03 it would not be appropriate to restrict applicant only to the previously elected species of invention (which is now canceled from the currently pending claims)."

   In response to the outstanding restriction requirement applicant states the following (applicant's emphasis shown):

   "Applicants disagree with this assertion, noting that claim 2 recites "the method comprising," indicating that the method comprises the culture of NKT cells with the proteins or the cell, along with any other treatment. That other treatment could include NKT cell culture in the presence of the other of the proteins or cell. To clarify that the Applicants do not wish to preclude the culture of NKT cells in both proteins and cells, claims 2 and 3 were amended to recite "...said modulation being mediated by (a) proteins extracted from tissue affected by the immune-related disorder, ~~or~~ (b) at least one liver-associated cell of a tolerized or non-tolerized subject[[s]] suffering from said immune-related or immune-mediated disorder or of said mammalian subject, or (c) a combination thereof."

Applicant then elects three species, without traverse, wherein the modulation is mediated by "proteins extracted from tissue affected by the immune-related disorder," wherein said proteins are "allogeneic antigens" and wherein said method involves culture condition that do "not include at least one cytokine."

As a preliminary matter, the examiner disagrees with applicant's assertion that claim 2 as amended in the papers filed October 27, 2010 encompassed the applicant's originally elected species of invention in its breadth. In particular, applicant's argument that the comprising language of claim 2 as amended October 27, 2010 allows for inclusion of, e.g., "NKT cell culture in the presence of the other of the proteins or cell" is not convincing because claim 2 as presented in the papers filed October 27, 2010 by the explicit words used encompasses two embodiments – method comprising culturing NKT cells in the presence of "proteins" OR "liver-associated cells". Anything else that is included in this open-ended method ("comprising…") cannot contradict the explicitly recited elements of the claim culturing NKT cells in the presence of "proteins" OR "liver-associated cells".

That said, consistent with applicant's "wish to preclude the culture of NKT cells in both proteins and cells," the claims as most recently amended do encompass in their breadth a method comprising an embodiment encompassing the culture of NKT cells in both proteins and cells.

In making said amendment applicant has obviated the need for the Restriction Requirement mailed April 18, 2011 because the claims as currently amended encompass the originally elected species of invention in their breadth.

Therefore, the Restriction Requirement mailed April 18, 2011 is hereby VACATED.

Please note that applicant's claim amendments filed October 27, 2010 and May 18, 2011 prompted the Restriction Requirement mailed April 18, 2011 and then rendered it moot, respectively.

3. Claims 1-3, 5-7, 9-11, 13, 16-18, 20, 23, 25-46, 50-63, 66-72, 83-126, 143, 152-164 and 167-186 are pending.

Claims 1, 5, 16-18, 20, 23, 25-29, 33-46, 50-63, 66-72, 83-126, 143 and 152-164 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

New claim 167 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group (Group III), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Moreover, new claims 168 and 177 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Furthermore, new claims 185 and 186 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of disease, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Thus, in summary claims 1, 5, 16-18, 20, 23, 25-29, 33-46, 50-63, 66-72, 83-126, 143, 152-164, 167, 168, 177, 185 and 186 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Claims 2, 3, 6, 7, 9-11, 13, 30-32, 169-176, 178-184 are under consideration wherein the species of "culture conditions for the ex vivo education of NKT" includes "allogeneic antigens obtained from donors suffering from said immune-related or immune-mediated disease", "Kupffer cells" and "IL4" and the species of "immune-related or immune-mediated disorders or diseases" is "autoimmune liver disease" or "Crohn's disease."

4. The prior rejection under 102(b) has been withdrawn in view of applicant's amended claim to the benefit of a prior filed application.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2, 3, 6, 7, 9-11, 13, 30-32, 169-176, 178-184 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment of TNBS-induced-colitis in a first mouse in need of such treatment comprising: (1) orally administering to said first mouse colitis extracted proteins (CEP) prepared from colons that were removed from TNBS-induced-colitis mice, cut into small strips, mechanically homogenized, filtrated through a 40 mm nylon cell strainer, and the colitis extract supernatant separated from intact cells via centrifugation; (2) obtaining 0.5×10^6 liver associated lymphocytes and 2.5×10^6 splenocytes from a second mouse that had been treated with TNBS to induce colitis and had been orally administered CEP prepared as in step (1); (3) adding to a culture of the 0.5×10^6 liver associated lymphocytes and 2.5×10^6 splenocytes from step (2) antigen presenting cells and CEP prepared as in step (1); (4) optionally adding to said culture IL4, IL10, TGFβ, IL18 or IL15, (5) administering the

cultured cells of step (3) to the first mouse in need of such treatment to modulate the Th1/Th2 balance toward anti-inflammatory cytokine producing cells, resulting in an increase in the quantitative ratio between any one of IL4 and IL10 to IFNγ

does not reasonably provide enablement for

a method for the treatment of Crohn's disease or autoimmune liver disease in ***any*** mammalian subject in need of such treatment, by manipulating ***any or all*** NKT cell population(s) of said subject, wherein manipulation of said NKT cell population(s) results in modulation of the Th1/Th2 cell balance toward anti-inflammatory cytokine producing cells, said modulation being mediated by ***any*** allogeneic antigens extracted from tissue affected by the immune-related disorder in the presence of at least one Kupffer cell and IL-4.

Applicant makes a number of arguments about why the instant claims were enabled as of applicant's date of invention.

Applicant's arguments have been considered, but have not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed April 27, 2010.

Applicant points to example 7 at pages 79-86 of the instant specification assertedly showing that "culturing NK1.1+ T cells in the presence of disease associated antigens (subgroup E"5) leads to cytokine pattern that is similar to that of tolerized cells as manifested by increase IL10 secretion." (Specification, p. 81, bottom).

In conjunction with this applicant states "It is further noted in this regard that the claims as amended do not recite 'resulting in an increase in the quantitative ratio between any one of IL4 and IL10 to IFNγ,' but do recite that the Thl/Th2 cell balance is modulated toward an anti-inflammatory response. While an increase in the quantitative ratio between any one of IL4 and IL10 to IFNγ is one way of measuring the effectiveness of the NK1.1+ education process, the effectiveness of that process, i.e., the modulation of the Thl/Th2 cell balance toward anti-inflammatory cytokine producing cells, can also be measured by evaluating the absolute measurement of IL4 and IL10 vs. IFNγ, for example as discussed in Example 7, e.g., at page 81: 'ex vivo education was examined by measuring secretion of IL10 (as compared to IFNγ secretion) by the different treated cells.'"

Applicant's argument is noted but, with regard to this line of reasoning in particular it is the examiner's position that even with the limitation about the claimed method modulating "the Thl/Th2 cell balance toward anti-inflammatory cytokine producing cells, resulting in an increase in the quantitative ratio between any one of IL4 and IL10 to IFNγ," no longer presently claimed it remains the case that the skilled artisan considering the finding of Example 7 as shown in Table 6 would be unclear if the NKT cells of the E''5 experimental group are truly educated to be anti-inflammatory when considering their IL-10/IFNγ ratio relative to, e.g., the NKT cells of E''2 animal.

This is because as stated in the prior Office Action mailed April 27, 2010 at page 4, 5th and 6th paragraphs:

"the teachings of the instant specification as a whole and the knowledge in the art collectively suggest the skilled artisan would not discount the increased IFNγ secretion and would consider the ratio of IL-10/IFNγ highly relevant to the use of the 'educated' cells in any future in vivo therapy.

For example, the working examples of the instant specification other than Example 7 report the value of the IL4 and IL10 to IFNγ ratio as a means of measuring the pro- or anti-inflammatory nature of NKT cells (see, e.g., Figures 2, 3, 5 and 9). This is consistent with the knowledge in the art where Th1/Th2 cytokine ratios are commonly measured (see, e.g., Zhou et al., J Clin Invest. 1998 Apr 15;101(8):1717-25, page 1722, Table III, cited herewith; Chiaramonte et al., Hepatology. 2001 Aug;34(2):273-82, page 276, right column, 1st paragraph, cited herewith)."

Applicant further argues "[t]he Office Action also asserts that the claims are not enabled because Applicants do not know what particular component of the CEP affected the NK T cells. In response, Applicants first note that there is no requirement under 35 U.S.C. 112, first paragraph, that the applicant must know the precise mechanism of how an invention works. All that is necessary is that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)." MPEP 2164.01(b). In the present case, Applicants assert that knowledge of the particular CEP component that affects the NKT cells is not necessary, because the skilled artisan would understand that "proteins extracted from tissue affected by the immune-related disorder" as claimed would be effective. As such, given the success of the CEP in educating the NKT cells in the exemplified inflammatory bowel disease case, the skilled artisan would understand that tissue affected by any other immune-related disorder likely has proteins that, when extracted from the tissue, would educate NK T cells ex vivo that, when reintroduced into the subject, would modulate the Thl/Th2 cell balance toward anti-inflammatory cytokine producing cells. Additionally, such a treatment could be tested with any particular immune-related disorder without undue experimentation by using the methods analogous to those described in the instant specification."

Applicant's argument is not found convincing for a number of reasons.

First, as stated in the prior Office Action mailed April 27, 2010 at page 6, 1st paragraph the issue is *not* that "applicant must know the precise mechanism of how an invention works" for enablement.

Rather, the issue is that while the skilled artisan need not know what "particular biomolecular constituent" (or constituents) of "colitis extracted protein" is/are responsible for mediating ex

vivo education of NKT cells in order to practice the *enabled* embodiment of the claimed method put forth in the header to the instant Section, without any knowledge as to what constituent(s) is/are required for the NKT cells to be educated as claimed, how is the skilled artisan to extrapolate these teachings to making use of any "allogeneic antigens extracted from tissue affected by the immune-related disorder" to ex vivo educate NKT cells without resorting to undue experimentation?

This point was illustrated by the following quote from the prior Office Action mailed April 27, 2010 at page 6:

"…without knowledge of what antigen(s) is/are capable of ex vivo educating NKT cells as claimed, the skilled artisan would have little hope of reliably predicting if any particular disease can even be a source of epitope or antigen that can be used in the claimed method.

For example, consider the immune-related disorder psoriasis. Some antigens or epitopes known to be associated with this disease are K13, hnRNP A1 and FLJ00294 (see Jones et al., J Invest Dermatol. 2004 Jul;123(1):93-100, in particular page 98, cited herewith). However, none of these antigens were/are known to stimulate NKT cells, and there is no expectation in the art that they would do so because these ligands were not known to bind CD1d, and would have been considered just as unlikely as any other randomly chosen polypeptide to activate CD1d-independent NKT (see, e.g., Godfrey et al., Immunol Today. 2000 Nov;21(11):573-83, in particular page 577, left column, 2nd-3rd paragraphs, cited previously).

Thus, this example illustrates how the skilled artisan would not know how to proceed to practice the claimed invention with a reasonable degree of predictability for any given disease, e.g., psoriasis."

Further consistent with the uncertainty the skilled artisan would face in attempting to extrapolate, with any reasonable degree of predictability, from the teachings of Example 6 to using any "allogeneic antigens extracted from tissue affected by the immune-related disorder" to ex vivo educate NKT cells without resorting to undue experimentation, as put forth in multiple prior Office Actions (see, e.g., April 27, 2010 at page 5), "…neither the instant specification nor the art seem to recognize what particular biomolecular constituent of the 'colitis extracted protein,' i.e., which epithelial cell or host microbial cell component, e.g., polypeptide and/or nucleic acid and/or lipid etc., is effecting NKT cells (see, e.g., Lee et al., Am J Gastroenterol. 2000 Apr;95(4):861, left column, 3rd paragraph and Kiron Das et al., Am J Gastroenterol. 2006 Dec;101(12):2889-90 and Margalit et al., Am J Gastroenterol. 2006 Dec;101(12):2890-91, in particular page 2890, right column, 2nd paragraph)(all cited previously)."

Thus, if the immune-related disorder to be treated is autoimmune liver disease, what would lead the skilled artisan to believe allogeneic proteins extracted from the liver would have the same effect as protein extracted from the tissue affected in Crohn's disease? For example, what if the biomolecular constituent present in CEP that allegedly educates NKT cells to be

anti-inflammatory is specific to the specialized structure / microenvironment of the intestinal tract such as a microbial cell component?

Additionally, given the uncertainty as to what particular biomolecular constituent found in CEP prepared from the colons of TNBS-induced-colitis mice is allegedly able to ex vivo educate NKT cells to be anti-inflammatory the skilled artisan would further consider the method used to prepare the extract to be used to ex vivo educate the NKT cells to be of the utmost importance.

However, other than teaching the preparation of an extract from colons removed from TNBS-induced-colitis mice, cut into small strips, mechanically homogenized and filtrated through a 40 mm nylon cell strainer (see Example 7) the instant specification offers the skilled artisan no further guidance as to what steps will produce a "protein extract" capable of being used as claimed.

In this regard applicant further argues, "Furthermore, the skilled artisan would understand that the procedure disclosed on page 61, 3rd paragraph would allow the skilled artisan to practice the invention as claimed, and that other extraction procedures, e.g., a detergent extraction as posited in the Office Action, could be tested without undue experimentation. The skilled artisan would also understand that there would likely be a number of extraction procedures that would obtain proteins that are useful for the present invention. Thus, the specification provides adequate guidance for the skilled artisan to practice the invention without undue experimentation."

This is not found convincing for a variety of reasons.

First, neither the instant specification nor applicant provides any objective evidence that "any number of extraction procedures…would obtain proteins that are useful for the present invention."

Secondly, the instant claims and applicant's arguments emphasize the importance of certain "proteins" in educating the NKT cells and yet, based on the objective evidence of record, it is the examiner's position that the skilled artisan would be entirely uncertain what the critical biomolecular constituent is of the extract prepared according to the procedure disclosed on page 61, 3rd paragraph of the instant specification (i.e., which epithelial cell or host microbial cell component, e.g., polypeptide and/or nucleic acid and/or lipid etc., is allegedly able to ex vivo educate NKT cells to be anti-inflammatory, see above).

Thirdly, it is not a matter of routine experimentation to test the genus of extraction procedures until one possibly arrived at the desired result in absence of any guidance or direction from the specification as to which parameters are critical or to which of many possible choices is likely to be successful.

Applicant further argues "the skilled artisan would not have understood the plasticity of NKT cells as described in Ilan 2009 at the time of filing."

Upon further consideration the examiner agrees with applicant's assertion that "the skilled artisan would not have understood the plasticity of NKT cells as described in Ilan 2009 at the time of filing."

That said, the instant claims remain non-enabled essentially for the reasons of record as described above. Moreover, it is worth noting that while much of what is discussed above focuses on the lack of enablement for the ex vivo education of NKT cells as claimed, the claims themselves are drawn to methods of treating "immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment" comprising administering the ex vivo educated NKT cells to said mammalian subject. However, the instant specification provides no working example showing the ex vivo educated NKT cells of example 7 (E''5) can indeed be used to treat an "immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment."

With regard to extrapolating experimental results obtained in mouse ex vivo educated NK 1.1+ T cells to human CD56+ NKT cells, applicant asserts "the essential similarities between human and mouse NK T cells for the purposes of the present invention outweigh the differences, such that the skilled artisan would believe that the mouse model utilized in the Examples is sufficiently predictive of human results such that the claimed methods would be expected to be effective in humans." (see remarks page 31, 2nd paragraph). In support of this argument applicant cites Galli et al., published June 2003 and Wilson and Van Kaer, Abstract only, published January 2003.

Applicant's arguments have been carefully considered but have not been found convincing.

First, the teachings of Galli and Van Kaer cited by applicant were published in 2003 prior to the filing date of the instant application but well after the effective filing date of 10/451,811 application (December 24, 2001) to which the instant application claims the benefit of priority. Thus the teachings of Galli and Van Kaer cannot be said to represent information the skilled artisan would know prior to applicant's earliest date of invention. Should applicant wish to declare that the earliest date of invention of the claimed method is with the filing date of the instant application, applicant should explicitly do so on the record.

That said, even after considering the teachings of Galli and Van Kaer the examiner disagrees with applicant's assertion that "the essential similarities between human and mouse NK T cells for the purposes of the present invention outweigh the differences, such that the skilled artisan would believe that the mouse model utilized in the Examples is sufficiently predictive of human results such that the claimed methods would be expected to be effective in humans," essentially for the reasons of record as put forth in the Office Action mailed April 27, 2010, in Section D, pages 9-11.

In this regard it is noted that the teachings of Galli provide no teachings specifically addressing the extensive differences between murine NK 1.1+ T cells and human CD56+ NKT cells.

Moreover, Van Kaer is provided in Abstract form only so what it would truly teach to the skilled artisan, when considered in its entirety, cannot be examined.

Lastly, applicant argues "[c]ertainly, the success of the use of tissue extracts in (a) the oral tolerization to colitis, as described in Example 1 at pp. 68-70, and (b) to hepatitis, as described in Example 6 at pp. 104-106, would have given the skilled artisan at the time of filing the understanding that the claimed methods were enabled much more than a reference discussing oral tolerization with a different antigen than claimed, or two references that were not published at the time of filing."

Applicant's arguments have been considered, but have not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed April 27, 2010 and for the reasons given below.

The instant claims are drawn to:

A method for the treatment of immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment, the method comprising manipulating the NKT cell population of said subject, wherein manipulation of said NKT cell population results in modulation of the Th1/Th2 cell balance towards an anti-inflammatory response, said modulation being mediated by (a) proteins extracted from tissue affected by the immune-related disorder, (b) at least one liver-associated cell of a tolerized or non-tolerized subject suffering from said immune-related or immune-mediated disorder or of said mammalian subject, or (c) a combination thereof, wherein the method comprises the steps of:

a. obtaining NKT cells from said mammalian subject or another subject;

b. ex vivo educating the NKT cells obtained in step (a) such that the resulting educated NKT cells may modulate the Thl/Th2 cell balance toward anti-inflammatory cytokine producing cells; and

c. re-introducing to said subject the educated NKT cells obtained in step (b),

and further comprising orally administering the proteins to the subject.

The instant specification provides a working example where TNBS-induced-colitis in a mouse is treated by orally administering colitis extracted proteins prepared from colons that were removed from TNBS-induced-colitis mice, cut into small strips, mechanically homogenized, filtrated through a 40 mm nylon cell strainer, and the colitis extract supernatant separated from intact cells via centrifugation, see specification pages 68-70.

However, this embodiment does not enable the breadth of the claimed method of treatment comprising administering any proteins extracted from any tissue affected by any immune-related disorder essentially for the reasons of record. In particular, as stated in the prior Office Action mailed April 27, 2010 the prior art teaches a number of large, rigorous and definitive clinical trials and failures of oral antigen immunotherapy as taught by Pozzilli and Wiendl. Thus, the field of oral antigen immunotherapy was at best highly unpredictable and at worst totally unsuccessful.

Applicant asserts that the teachings of Wiendl (2002) and Margalit (2006) cannot be properly considered to support the unpredictability of the field of oral tolerization because they represent post-filing date art.

Applicant's argument is not found convincing because as stated in the prior Office Action mailed September 9, 2008, Wiendl pages 194-195 describes how orally administered bovine myelin basic protein showed no significant medical effect in a consecutive multicenter, double-blind, placebo-controlled phase III study of 516 patients with relapsing-remitting MS, a finding known prior to applicant's date of invention.

Moreover, the teachings of Margalit were cited and argued by applicant themselves as supporting enablement (see remarks filed March 9, 2009).

Applicant further argues Pozzilli would not indicate anything to the skilled artisan about the effectiveness of "proteins extracted from tissue affected by the immune-related disorder."

This argument is not found convincing because insulin is a protein extracted from tissue (i.e., pancreas) affected by an immune-related disorder (i.e., diabetes).

Applicant further points to example 6 at pages 105-106 as disclosing a working example showing oral tolerization to hepatitis; however, it is unclear from this disclosure what effect liver extract has on wild-type mice or what the effect of liver extract feeding on ob/ob mice has to do with treating autoimmune liver disease.

In conclusion, the instant claims encompass an invention of tremendous breadth, and essentially call for trial and error by the *skilled artisan to begin discovering how to practice the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.*

The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Undue experimentation would be required to practice the invention commensurate with the breadth of the claims based on the disclosure of the instant specification and the knowledge

in the art. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed method of treatment.

7. The following is a New Grounds of Rejection necessitated by applicant's claim amendments.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2, 3, 172 and 173 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
9.

Claim 172 recites "a method for the treatment of immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment, the method comprising manipulating the NKT cell population of said subject, wherein manipulation of said NKT cell population results in modulation of the Th1/Th2 cell balance towards an anti-inflammatory response, said modulation being mediated by ***(a) proteins extracted from tissue affected by the immune-related disorder,*** (b) at least one liver-associated cell of a tolerized or non-tolerized subject suffering from said immune-related or immune-mediated disorder or of said mammalian subject, or (c) a combination thereof, ***wherein said tissue is healthy tissue."***

Claim 173 recites "a method for the treatment of immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment, the method comprising manipulating the NKT cell population of said subject, wherein manipulation of said NKT cell population results in modulation of the Th1/Th2 cell balance towards an anti-inflammatory response, said modulation being mediated by ***(a) proteins extracted from tissue affected by the immune-related disorder,*** (b) at least one liver-associated cell of a tolerized or non-tolerized subject suffering from said immune-related or immune-mediated disorder or of said mammalian subject, or (c) a combination thereof, ***wherein said tissue is tissue diseased from the immune-related or immune-mediated disorders or diseases."***

With respect to claim 172, it would be unclear to the skilled artisan how "tissue affected by the immune-related disorder" could also be "healthy tissue." Is the skilled artisan supposed to draw a healthy / unhealthy distinction between different types of "tissues affected by the immune-related disorder," and if so, what would be the basis for such a distinction?

With respect to claim 173, how does the "wherein said tissue is tissue diseased from the immune-related or immune-mediated disorders or diseases" further limit the base claim, i.e.,

what is distinction between "tissue affected by the immune-related disorder" and "tissue diseased from the immune-related or immune-mediated disorders or diseases?" Put another way, claim 173 is unclear in much the same way as claim 172.

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/
Primary Examiner, Art Unit 1644